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DEPARTMENT OF SUMMARIES

TO BE DEVOTED TO DIGESTS OF PROGRESS IN BIOLOGY

While the *Transactions* will continue to be primarily a Journal of research in micro-biology, it is recognized that the field has become so broad as to preclude the possibility of frequent articles in any one of the departments of special interest. Because of this it will be the policy to present, from time to time, supplementary digests of the progress being made in the various fields of micro-biology. It is also proposed to introduce similar summaries of the progress made in some departments not represented in our articles of research. This is done with the feeling that such reviews will increase the permanent value of the *Transactions* to all who may not have access to a large list of technical biological journals, nor the time to make the survey for themselves.

RESULTS OF RECENT STUDIES OF THE MAMMALIAN EPIPHYSIS CEREBRI

By H. E. Jordan

The last decade has witnessed great activity in the study of the "organs of internal secretion", notably the hypophysis. The definite results here obtained have stimulated renewed interest in that enigmatical body, the conarium or epiphysis cerebri. The investigation of this organ has been approached from various directions, namely, histological, histogenetic (embryological), pathological, clinical and experimental (physiological). In view of certain contradictory histological and experimental results, it seems premature to speak of a pineal "gland". Certain gross and microscopical morphological characters recall glandular tissue; but the absence of excretory ducts vitiates the strict analogy. Certain other characters (e. g. cysts or blind alveoli, profuse vascularity) suggests an organ of internal secretion. It is the main purpose of this paper to record, and briefly analyze, the findings which have been reported for and against physiological significance, and to determine the present state and general trend of our knowledge of the pineal organ of mammals. Certain details, of only subsidiary significance from the standpoint of our chief object, may properly be neglected. Nor need comparative morphological observations be here noted. As regards cytological and histological facts, only those will be specially considered that indicate or contravert glandular activity. A summary of progress made will serve the better to indicate what still awaits solution, and, in a measure, suggest the best methods of further approach.

HISTOLOGICAL STUDIES

Since histological observations would seem to be simplest and therefore least liable to differences of interpretation, the analysis logically considers these first.

With modern technique Dimitrova[1] (1901) carefully studied the pineal bodies of a number of the common domestic mammals, and arrived at the conclusion that the parenchyma consists of a single cell type, a neuroglia cell. Cysts, pigment granules, brain sand, and a few striped muscle cells (ox) were also described in certain forms and in varying quantities. Certain cytoplasmic granules and vacuoles of uncertain significance, but suggestive of secretion, were also noted. The point of prime importance, however, pertains to the conclusion that the earlier[2] identification of several (two to four) different types of parenchymal cells is untenable. Nor could Dimitrova identify ganglion cells. On a basis of a histogenetic study of the pineal organ of the sheep, Jordan[3] (1911) confirms Dimitrova's findings respecting a single type of parenchymal cell. Costantini[4] (1910) on the contrary, describes "acidophile" and "basophile" cells, the presence of which he interprets as indicating an internal secretory function.

The neuroglia parenchymal cells frequently contain melanic granules (e. g. young sheep; Jordan[5]). Dimitrova[6], and Pappenheimer[7] (1910), moreover, describe colloid spherules in the cytoplasm. Such are certainly not present in sheep. In the latter, fat vacuoles frequently appear. Bailey and Jelliffe[8] (1911) state that "histologic evidence points to the fact that this structure (pineal body) contains elements which ally it to the blood glands—the chromaffine system—and that like other members of this series, the hypophysis, thymus, thyroid, and adrenals, etc., it plays a part in trophism". But a careful search for phaeochrome granules in the pineal body of the sheep gave me only negative evidence. Though the pineal is by some included in the "chromaffine system", I know of no positive cytological evidence of a "chromaffine reaction" of any parenchymal cells, hence its classification as a "blood-gland" (von Cyon[9]; 1910) seems unwarranted.

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[1] Dimitrova, Z. (1901)—Recherches sur la structure de la glande pinèali chez quelques mammifères. Le Neuraxe 2:3.

[2] The earlier histological literature is fully reviewed in the works of Studnicka (Oppel's Lehrbuch, 1905), Dimitrova, and Cutore; the pathological and clinical literature in the paper by Bailey and Jelliffe, loc. cit.

[3] Jordan, H. E. (1911)—The Histogenesis of the Pineal Body of the Sheep. Amer. Journ. of Anat., 12:3.

[4] Constantini, G. (1910)—Pathologica, 2:45. Ref. Neurol. Centrbl., Aug. 1, 1911.

[5] loc. cit.

[6] loc. cit.

[7] Pappenheimer, A. M. (1910)—Ueber geschwülste des Corpus pineale. Virchow's Archiv für path. Anat. und Phys., Bd. 200.

The sparse sensory nerve supply is limited to the proximo-ventral and proximo-dorsal portion of the structure; and the sympathetic to the blood vessels. The proximo-dorsal bundle from the superior commissure, may represent the parietal (pineal) nerve of lower forms. The body is very vascular. It is roughly divided by pial trabeculae into lobes and lobules (follicles). Commonly, mammalian pineals contain ependyma-lined cysts, clumps of pigment, and brain sand (acervulus), all of which features vary greatly according to form, and more especially according to age. Cysts and intracellular pigment granules are more numerous in youth, clumps of intercellular pigments and brain sand in advanced age. Pigment in the adult pineal seems to be most abundant in the horse (Dimitrova[10]).

Histological marks in general indicate a progressive involution with age, beginning about the time of puberty—about seven years in man (Bailey and Jelliffe[11]); about 8 months in sheep (Jordan[12]). This histological involution is accompanied by decrease in size.

Illing[13] (1910) has described a few smooth muscle cells in the finer trabeculae (ox). Ganglion cells, and occasional striped muscle cells (ox and calf; Nicholas[14], 1900, and Dimitrova[15]) are possibly to be interpreted as teratomatous in nature. The pineal body, in common with rudimentary structures, seems especially prone to teratomata. Possibly the various nuclear and cytoplasmic phenomena (e. g. basophile and acidophile granules, vacuoles, "colloid spherules," etc.), on the basis of which the parenchymal cells have been classified as of several distinct types, have only degenerative significance.

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[8] Bailey, P. and Jelliffe, S. E. (1911)—Tumors of the Pineal Body. Archiv f. Int. Med. 8:6.

[9] v. Cyon, E. (1910)—Die Gefässdrüsen als regulatorische Schutz organe des Zentral, nervensystems. Berlin.

[10] loc. cit.

[11] loc. cit.

[12] loc. cit.

[13] Illing, P. (1910)—Vergleichend Anatomische und Histologische Untersuchungen ueber die Epiphysis cerebri einiger Säuger. Inaug. Diss. Leipzig.

Judged from structural marks, the pineal body has small functional value, limited to late foetal or early post-natal (pre-pubertal) life.

In view of the fact that striped muscle is the only mesodermal element that has been described in the supposedly normal pineal parenchyma, and this only occasionally and in very small amount, it may possibly be that cells so interpreted are in reality enlarged fusiform or rectangular elements which, by reason of a regular arrangement of the cytoplasmic granules, simulate a striped muscle-cell appearance. Otherwise, if, and where, actually present, the pineal is probably teratomatous.

The cytoplasmic melanic granules of foetal and young stages (sheep) must probably be interpreted in terms of the phylogenetic history (regression) of the pineal organ. Tendency to pigment elaboration may be a survival of the ancestral condition when the pineal functioned as an "eye" (light perceptive). An alternative interpretation might regard the melanic granules as secretory products in a transient phase as a chromatic proteid (Dyson[16], 1911), the vacuoles representing the decomposition phases. The pigment clumps of old pineals probably signify degeneration products.

The cysts also may have only ancestral significance; for they are especially numerous and well developed in certain birds. Since they are in communiction during no portion of the developmental history of the pineal either with the surface or the recess, however, they are the more difficult of interpretation. Moreover, they seem filled with a very dilute fluid. Indeed, the cysts appear to have origin through the accumulation of fluid forcing the arrangement of the parenchymal cells for a time into alveoli-like structures. The fluid may possibly be lymph, which has escaped from the large perivascular lymph spaces.

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[14] Nicolas, M. (1900)—Note sur la presence des fibres musculaires striees dans la glande pineale de quelques mammiferes. Compt. rend de la soc. de biol., Paris.

[15] loc. cit.

[16] Dyson, Z. (1911)—An Investigation on Cutaneous Pigmentation in Normal and Pathological Conditions. Journ. Path. and Bact. 15:3.

PATHOLOGICAL STUDIES

All the more complete histological descriptions of pineal tumors identify several types of cells more or less distinct. In a large pineal tumor (ca. 3.5 cm. dia.), for which the term "neuroglia ependymale" is suggested, Pappenheimer[17] describes besides neuroglia cells, "neuroblast-like cells", "ependyma-like cells" and embryonal striped muscle cells. The latter are very few in number, and found only in several sections. The cytoplasm of the several cell types is said to be frequently vacuolated and to contain "colloid" spherules.

In a large tumor (1.5 in. dia.) replacing the pineal body, Bailey and Jelliffe[18] describe hair and cartilage. Teratomata of the pineal body are described also by Neumann[19] (1900), Marburg[20] (1909; mixed tumor), and Frankl-Hochwart[21] (1909). Other neoplastic growths, replacing the pineal, include epithelial carcinoma, neuroglioma, sarcoma, adenoma, choric-epithelioma, gliosarcoma, hemorrhagic angiosarcoma, glioma, and gliosarcoma[22]. The frequency of a pure or mixed gliomatous condition among pineal tumors is significant. Indeed, the adult pineal is normally essentially a mass of neuroglia cells, i.e., practically a small or potential glimoa. In view of the frequent presence of considerable quantities of pigment, coupled with the tendency to neoplastic alterations, the absence of melanotic tumors of the pineal seems remarkable.

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[17] loc. cit.

[18] loc. cit.

[19] Neuman, P. (1900)—Ein neuer Fall von Teratom der Zirbeldrüse. Inag. Diss. Königsberg.

[20]. Marburg, O. (1909)—Zur Kenntnis der normalen und pathologischen Histologie der Zirbeldrüse, Die Adipositas cerebralis. Arb. a. d. Wiener Neurol. Institut, 17.

[21]. Frankl-Hochwart, L. (1909)—Ueber Diagnose der Zirbeldrüsentumoren. Deutsch. Ztschr. f. Nervenh., 37.

[22]. For review of these cases of pineal tumors and list of literature see Bailey and Jelliffe.

EMBRYOLOGICAL STUDIES

The pineal body arises as an ependymal diverticulum from the roof of the diencephalon. In the sheep (Jordan[23]) of the 5 cm. stage of development the ependymal cells of this apically thickened pocket are actively proliferating and undergoing the early differentiation processes in the formation of neuroglia and inter-neuroglia (less differentiated neuroglia) cells. Both types (stages) contain abundant small spherical melanic granules. At half term (21 cm.) the body is filled with blind cysts, lined with tall columnar (ependymal) cells. The cysts in sections contain a coagulated fluid. They progressively disappear, only a few persisting to birth and occasionally after. Cutore[24] (1911) records histological observations on certain embryonic and foetal stages in ox and man. He also recognizes originally only neuroglia (differentiated from ependyma) cells; but he describes a secondary differentiation into cells with "epithelial character" and "lypmhatic elements."

Cytological findings in the sheep give no evidence of secretory function. Cutore, on the contrary, maintains that an organ of such complex structure, constituted of neuroglia, epithelial, and lymphatic tissue, with tubular cavities, pigment cells, calcareous concretions, and a rich blood supply is not in a condition of regression. He believes that these structural characteristics warrant attributing to it the significance of a glandular organ with an internal secretion. However, the evidence presented for internal secretion seems far from adequate to the demands of a demonstration.

CLINICAL STUDIES

A very interesting and suggestive feature of pineal investigation relates to the clinical symptoms accompanying a tumor condition of this organ. Frankl-Hochwart[25] (1909) first directed special attention to the possible influence of the pineal body in cases of young individuals who showed—besides the ordinary tumor symptoms and those accompanying diseases of the corpora quadrigemina—abnormal size, extraordinary hair growth, obesity, drowsiness, premature genital and sexual development, and mental precocity. Marburg[26] (1908-1909) had previously called attention to a possible relation between pineal tumor (hypopinealismus) and adiposis, "adipositas cerebralis". Examination of the clinical histories of the cases mentioned at the close of a previous section, "Pathological Studies", shows that the symptoms accompanying disease of the pineal organ are adiposis, early sexual maturity, and cachexia.

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[23] loc. cit.

[24] Cutore, . (1911)—Il corpo pineale di alcuni mammiferi. Archivio Italiano di Anatomia e di Embryologia, 9: 3 and 4.

[25] loc. cit.

Illustrative of typical cases of diseased pineal are two described by Pellizzi[27] (1910) under the title, "Makrogenistomia praecox": One, a child of 5 years, measured 127 cm. Already at the seventh month the abnormal development was evident. At 2 years his genetalia were like those of an adult, and erections and ejaculations, with spermatozoa, occurred. Profuse pubic hair and beard were present. Radiographs indicated an age of about 16 years. The jaws, however, were infantile in character. A second patient was similar to the above, with hydrocephalus; and idiotic. Analysis of cases with similar symptom-complex reported by previous observers, and checked at necropsy, leads Pellizzi[28] to the hypothesis that the syndrome present in his cases relates to changes in the pineal body. He gives also a critical differential diagnosis between the pineal syndrome and the symptom-complex of pituitary disturbance (dyspituitarism).

An interesting complication arises from the fact that disease of the hypophysis also causes adiposis. Why should a pineal tumor produce the identical result? A possible explanation is as follows: a pineal tumor may block the aqueduct of Sylvius, and thus produce internal hydrocephalus, with consequent pressure on, and atrophy of, the hypophsis. On the basis of the work notably of Paulesco[29] (1908) and of Cushing[30] (1909) it seems certain that hypopituitarism is associated with adiposis, genital atrophy and lack of sexual development; and that apituitarism is a concomitant of cachexia, usually leading to death. However, pineal tumors seem to cause also genital hypertrophy and sexual precocity, a condition associated likewise with hyperpituitarism. Thus a seemingly serious contradiction appears, which somewhat invalidates the explanation of symptoms associated with pineal tumor as an indirect effect on the hypophysis. Bailey and Jelliffe[31] suggest that "possibly here the type of tumor introduces new elements that must be reckoned with, and whereas adiposis may be a more general factor dependent on hypopinealism, or on hydrocephalus, the sexual precocity may be due to a specific type of tumor, namely to teratomata, or possibly also to adenomata" p. 859. They suggest still another possibility: "It may be that the precocious sexual development may be an early irritative sign of a purely nervous character acting through the pars nervosa sympathetic system, which is very rich, and that later increases in pressure brings about degeneration or atrophic phenomena. Further, Cushing's hypothesis which assumes that dyspituitarism results from lessened pituitary secretions in the cerebrospinal fluid, which results from pressure on the infundibulum, may be the explanation of these sexual changes". p. 859.

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[26] loc. cit.

[27] Pellizzi, G. B. (1910)—La sindrome "macrogenistomia praece." Riv. Ital. di Neuropatol., Psich. ed Eleccroterapia, 3:5—Ref. Neurol. Centrbl., Aug. 1, 1911.

[28] loc. cit.

[29] Paulesco, M. C. (1908)—L'Hypophyse du Cerveau, Vigot Frères, Paris.

[30] Cushing, H. (1909)—Partial Hypophysectomy for Acromegaly, with Remarks on the Function of the Pituitary Body. Ann. of Surg., 1903.

More specifically, Marburg[32] (1909) describes (a) universal adiposity as due to hyperpinealismus, (b) premature development of the genital organs or genital hypertrophy as due to hypopinealismus, and (c) cachexia as due to absence of pineal or apinealismus.

Kidd[33] (1910) points out that a and b are the exact reverse of hyperpituitarism and hypopituitarism. He suggests that there may be a "functional relationship between the pineal and the pituitary, the former's function waning as the latter's begins to wax". On this basis he explains the results of the hypophysectomy experiments on puppies by Crowe, Cushing and Homans[34] (1910), showing that puppies survived this operation much longer than adult dogs. He suggests that "the puppy's active pineal may secrete a substance that to some slight extent takes the place, physiologically, of his at present immature pituitary" p. 2003.

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[31] loc. cit.

[32] loc. cit.

[33] Kidd, L. (1910)—Pineal Experimentation. British Medical Journal, Dec. 24, 1910.

[34] Crowe, S. J., Cushing, H. and Homan, J. (1910)—Experimental Hypophysectomy. Johns Hopkins Bulletin 21:230.

EXPERIMENTAL (PHYSIOLOGICAL) STUDIES

The experimental work has naturally occupied itself with injections of pineal extract, and with attempts to extirpate the organ.

Injections of pineal extract were first made by von Cyon[35] (1903 and 1907) with the result of no effect on blood pressure and of irregular alterations in the force and frequency of the heart-beat, chiefly slowing it. He believed this effect due to the salts of the calcareous concretions. He further regarded the pineal as an organ designed to regulate mechanically, by contraction and relaxation, the pressure of the cerebrospinal fluid in the brain ventricles and incidentally cerebral blood pressure. That the possible functional significance of pineal extract does not depend upon the presence of the salts (calcium carbonate and phosphate) of the conconcretions seems strongly indicated by the fact of their increase with age, concomitant with the appearance of cytological and histological degenerative alterations.

Dixon and Halliburton[36] (1909) prepared in four different ways extracts of the pineal organ of 125 adult sheep. Injections were made intravenously into anaesthetized cats. They record a slight transient fall of blood pressure. They conclude that their work throws no light on the possible physiological action of the pineal body in mammals.

Jordan and Eyster[37] (1911) performed similar experiments with sheeps' pineal extract on dog, cat, sheep and rabbit. They record a uniform result of a slight fall of blood pressure, slight improvement in the beat of the isolated cat's heart, transient diuresis, and a slight irregular respiratory effect.

The foregoing results are again, in part at least, the reverse of those obtained with extracts of the hypophysis (anterior portion of pituitary body) and again suggests a compensatory or antagonistic regulatory functional relationship. Kidd further suggests pineal feeding and transplantation experiments. Extracts should also be tried upon completely hypophysectomized puppies to determine whether this might operate to prolong life.

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[35] v. Cyon, E.—Zur physiologie der Zirbeldrüse. Archiv für die gesammte Physiologie, 1903, p. 98, and Comptes rendus de l'Académie des Sciences, 1907, 144, p. 868.

[36] Dixon, W. E. and Halliburton, W. D.—Der Pinealkorper. Quar. Journ. of exp. physiol., 1909, II, p. 283.

[37] Jordan, H. E. and Eyster, J. A. E. (1911)—The Physiological Action of Extracts of the Pineal Body. Amer. Journ. of Physiol. 29:11.

Cytological study of the sheep's pineal organ has convinced me[38] that any possible secretory activity is limited to the young animal, or possibly also to the foetus. Accordingly it follows, in my opinion, that experimental work with extracts should be confined to those from young material. Kidd[39] urges the same point, and suggests that the question be investigated with extracts of the pineal of newly-born or very young rabbits, kittens, puppies or guinea-pigs. The experiments, he suggests, should be performed on two series of animals, namely (1) very young ones, and (2) adults. "It is possible that in the case of the former a condition of experimental hyperpinealismus might be induced; in the case of adult animals there should be subsequent microscopical examination of their pituitary, thyroid, parathyroid, adrenals and genital glands." The last suggestion made in this quotation assumes a close relationship between the pineal and the organs of internal secretion, for which assumption there is no basis of convincing histological or experimental data.

The association of hypopinealism with sexual precocity (a symptom also of hyperpituitarism) may perhaps be explained on the basis of the absence of an inhibitory (on pituitary growth) secretion of the pineal; or possibly simply the absence of the ordinary pressure prevalent during normal concomitant pineal and pituitary development.

Extirpation experiments have thus far been successfully performed in numbers only on rabbits. Exner and Boese[40] (1910) operated on 95, of which 22 survived, but only 6 lived to sexual maturity. Loss of pineal in these six gave no evidence of any effect on development or the appearance of sexual maturity.

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[38] loc. cit.

[39] loc. cit.

[40] Exner and Boese (1910)—Ueber Expérimentelle Extirpation des Glandula Pinealis. Deut. Zeit. f. Chir. October.

Sarteschi[41] (1910) studied the pineal in castrated animals (certain common mammals). He destroyed the organ by thermocautery. Castration showed no effect. Neither did the destruction by cautery give any noticeable effect. The pineal was removed in 11 rabbits. Only two survived the operation. The only result recorded is emaciation. One is suspicious, however, that this may have been a general post-operative condition rather than a specific effect of pineal absence.

Cats and dogs are impracticable for this operation due to the presence of an ossified tentorium, into a median notch of the lower border of which the pineal organ fits.

From every standpoint (except expense) the sheep (lamb) seems the most promising subject for this work. Numerous attempts have been made by several investigators to remove this body in the sheep but as yet without successful issue. As in cerebral surgery generally, profuse hemorrhage obscures the field and renders difficult the final step in the operation, i.e., clean and complete removal. This is a prohibitory detail, however, which it seems possible ultimately to circumvent.

Future attempts to elucidate the functional significance of the pineal body of mammals will find the most promising material in extracts, and extirpation experiments, of lambs. The influence of the extracts should be observed in young, old and hypophysectomized animals (sheep).

To date, a conservative estimate of all the evidence indicates very meagre, if any, functional activity, probably never essential to life. The practical absence of a pineal body in the opossum (Jordan[42], 1911), adds further support to this conclusion. Biedl[43] (1910), however, arrives at the conclusion that the pineal body is an organ of internal secretion with metabolic significance limited to the young. The clinical symptoms associated with pineal tumor are probably to be interpreted as symptoms of pressure on the corpora quadrigemina, or as due indirectly, through compression of the aqueduct and consequent third ventricle hydrocephalus, to disturbance of the pituitary body. The slight disagreement regarding histological details probably finds its explanation in the fact that the pineal body, in common with rudimentary organs generally, is the seat of regressive changes, and of some degree of teratomatous alterations[44].

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[41] Sarteschi, U.—Richerche istologische sulla glandula pinealse. Folia Neuro Biologica 4:6. Ref. Neurol. Centrbl. Aug. 1, 19.

[42] Jordan, H. E. (1911)—The microscopic anatomy of the epiphysis of the opossum. Anat. Rec., vol. 5, no. 7.

[43] Biedl, A. (1910)—Innere Sekretion, Berlin.

Anatomical Laboratory, University of Virginia.

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[44] Other recent papers not directly accessible dealing with the pineal organ are (a) Anglade et Ducos, 1908, Note préliminaire sur l'anatomie et la physiologie de la glande pinéale. Société d'Anat. et de Physiol. de Bordeaux, Proces. Dec. 14. (b) Calasescu et Urechia, 1910, Les cellules acidophiles de glande pinéale, Compt. rend. Soc. Biol. T. 68.; (c) Krabbe—Sur la Glande Pinéale chez l'homme. Nouvelle Iconographic de la Salpêtriere, Paris, 24 Année, no. 4. July, August 1911, p. 257-272.

SUMMARIES IN MICRO-BIOLOGY

For some months the Secretary has been planning to secure for this Journal and its Department of Summaries, a series of papers from biologists dealing with the chief groups of microscopic plants and animals. It has not been the purpose to present a complete survey of any of the groups. The wish has been rather to bring together in one article a statement of the following things:—general biology, the method of finding, the methods of capture and of keeping alive and cultivating in the laboratory; how best to study; the general technic; the most accessible literature; and a brief outline of the classification, with keys for the identification of at least the more representative genera and species of the micro-organisms likely to be found by the beginning students in the United States.

It has been felt that the getting together of such data as this, while not a contribution to science, would be a contribution especially to isolated workers and to teachers and students in the high schools and smaller colleges.

A paper has already appeared treating the aquatic Oligochetes. The following is the second paper of the series. It is proposed to have such synopses from time to time until the more common American species of such groups as the following have been covered: The Blue-green Algae, Conjugating Algae, Diatoms, other Green Algae, Zygomycetes, Downy Mildews, Yeasts, Powdery Mildews, Hyphomycetes, Smuts, Rusts; Rhizopods, Infusoria, Turbeliaria, Bryozoa. Water Mites, Entomostraca, etc.—[Editor.]